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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|----------------------------|-------------|----------------------|---------------------|------------------|
| 09/845,742 | 05/01/2001 | Wolfgang Picken | PRO.03 | 3461 |
| 25871 | 7590 | 04/19/2004 | EXAMINER | |
| SWANSON & BRATSCHUN L.L.C. | | | RILEY, JEZIA | |
| 1745 SHEA CENTER DRIVE | | | | |
| SUITE 330 | | | ART UNIT | PAPER NUMBER |
| HIGHLANDS RANCH, CO 80129 | | | 1637 | |

DATE MAILED: 04/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|-------------------------|------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 09/845,742 | PIEKEN ET AL. |
| | Examiner Jezia Riley | Art Unit 1637 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 17 March 2004.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-21 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-8,11-18 and 21 is/are rejected.

7) Claim(s) 9,10,19 and 20 is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. _____.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.

4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.

5) Notice of Informal Patent Application (PTO-152)

6) Other: _____.

DETAILED ACTION

Response to Remarks

1. Applicants' arguments and amendments, filed on 3/17/04, have been approved and entered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 1-8, 11-18, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Coolidge et al. (US5,221,736).

Coolidge et al. is directed to a method of purifying sequentially synthesized peptides and oligonucleotides by affinity techniques. Selected products are capped with an N-terminus capping agent for peptides or a 5'-terminus capping agent for oligonucleotides, and then bound with affinity agents that are selective for the corresponding capping agents.(Abstract).

In one embodiment, an acrylic acid or related derivative is employed as the capping agent. The acid is coupled to the selected peptide or oligonucleotide through an acid chloride or anhydride reaction. Thereafter, the capped, selected products are removed by either a Diels-Alder reaction in which the solid support in the purification carries a diene, such as maleic anhydride, or by the addition of a radical initiating reagent, such as ammonium persulfate in the presence of acrylamide or a solid support containing a double bond which will result in the formation of a polymer containing the failed peptide or oligonucleotide. (col. 16, lines 38-55, claim 13).

4. Claims 1- 8, 11-18, and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Pieken et al. (US 6,262,251 B1)

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Pieken et al. discloses methods for the synthesis and purification of oligonucleotides. In a preferred aspect of the invention a partitioning method to remove unreacted oligonucleotide starting material serves to both allow for the isolation for reuse of the unreacted oligonucleotide and also will result in a resin-bound

oligonucleotide product which is easily deprotected in preparation for the subsequent addition of the next 5'-protected monomer unit. Most preferably, the protecting group will covalently react with a derivatized solid support, such as a resin, membrane or polymer, to give a covalently anchored protecting group which may easily be cleaved from the oligonucleotide with high selectivity.

In the most preferred embodiment of the invention, the monomer unit consists of a 5'-protected phosphoramidite or H-phosphonate, wherein the protecting group is a substituted trityl group, levulinic acid group or silyl ether group. The preferred substitution on the protecting group is a diene functionality (which is viewed as the instant cap reagent), which can react, via a Diels-Alder reaction, with a solid support, such as a resin, membrane or polymer that has been derivatized with a dienophile. In this embodiment, the unreacted oligonucleotide starting material is separated from the reacted nucleotide product based on the selective or specific covalent reaction of the 5'-protecting group with a derivatized resin. (col.9)

A "solid support" as used herein refers to a resin, membrane, phase, polymer, polymer precursor, or soluble polymer that can undergo phase transition. A solid support also refers to a resin, membrane, phase, polymer, polymer precursor, or soluble polymer that has been derivatized with a D group. The term resin and solid support are used interchangeably and one of ordinary skill in the art will recognize what is intended by the term resin. Examples of solid supports include, but are not limited to, maleimide derivatized polystyrene, polystyrene derivatized with D groups, as defined below, dienophile or diene derivatized polystyrene. Tentagel.TM. derivatized with a D groups,

as defined below, dienophile or diene derivatized Tentagel.TM., dienophile or diene derivatized ultrafiltration membranes, dienophile or diene derivatized polyethylene glycol, diene or dienophile derivatized inorganic oxides, such as silica gel, alumina, controlled pore glass and zeolites, other dienophile or diene derivatized polymers, hydrophobic reverse phase resins, such as C2 to C18 polystyrene, thiopropyl Sepharose (Pharmacia Biotech), mercurated resin, agarose adipic acid hydrazide (Pharmacia Biotech), or avidin resin. (col.9).

After the unreacted monomer has been removed from the reaction mixture, the remaining filtrate may then be partitioned in any manner suitable to separate the "oligonucleotide product" from the "failure sequence." In one embodiment, the filtrate is applied to a material designed to interact selectively or specifically with the 5'-protecting group (D-E), such as a reverse phase resin. The product is captured or retained on the solid support by affinity of the 5'-protecting group constituent D with the resin. In a preferred embodiment, the filtrate is applied to a material designed to covalently react with the 5'-protecting group (D-E), such as a dienophile derivatized resin where D contains a diene unit (which is viewed as the instant trapping agent). The product is captured or retained on the solid support by covalent reaction of the 5'-protecting group constituent D with the resin. The unreacted oligonucleotide starting material 8, which does not carry the 5'-protecting group D, is washed away. The unreacted starting material may be isolated and stored to be used as an intermediate in a subsequent synthesis. The retained oligonucleotide product 9 is then released from the resin according to well known procedures. In certain embodiments, the oligonucleotide

product is released by cleavage of the bond between the 5'-oxygen and the protecting group D-E. For example, when the 5'-protecting group is a trityl derivative, a reagent such as dilute dichloroacetic acid (DCA) may be used to cleave the trityl group, thereby releasing the oligonucleotide coupling product. The liberated 5'-deprotected oligonucleotide coupling product 11 can then be used as the starting material in an additional coupling reaction. (col.16; scheme2, scheme 11).

D-E can be any group that enables the partitioning of the "growing oligonucleotide chain" or "oligonucleotide product" away from unwanted side products and starting materials. D includes, an alkyl or substituted alkyl group bearing a conjugated diene unit, an alkoxy or substituted alkoxy group bearing a conjugated diene unit, $\text{CH}_2 = \text{CHCH=CHCH}_2 \text{CH}_2 \text{O-}$, maleimide substituted alkoxy groups, dienophile substituted alkoxy groups, alkoxy groups, an alkylamino or substituted alkylamino group bearing a conjugated diene unit, maleimide substituted alkylamino groups or substituted alkylamino groups, an alkylarnino group or substituted alkylarnino group bearing a dienophile moiety, disulfides, aldehydes, and metal chelators. (col.10-12).

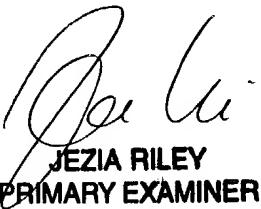
5. Claims 9, 10. 19 and 20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jezia Riley whose telephone number is 571-272-0786. The examiner can normally be reached on 9:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Thursday, April 15, 2004



JEZIA RILEY
PRIMARY EXAMINER